MAYO CLINIC LABORATORIES

Test Definition: BGAW

Beta-Galactosidase, Blood

Overview

Useful For

Diagnosis of GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis using whole blood specimens

This test is **not useful** for carrier detection.

Genetics Test Information

The beta-galactosidase enzyme is deficient in the following conditions: GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis.

Testing Algorithm

See Lysosomal Storage Disorders Diagnostic Algorithm, Part 1

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1

Method Name

Fluorometric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Additional Testing Requirements

Careful review of clinical findings will help distinguish between GM1 gangliosidosis and Morquio syndrome type B. A diagnosis of galactosialidosis must be additionally be ruled out (OLIGU / Oligosaccharide Screen, Random, Urine or LSDGP / Lysosomal Storage Disease Gene Panel, Varies).

Necessary Information

Provide a reason for testing with each specimen.

Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)
Specimen Volume: 2 mL

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	
	Refrigerated	7 days	

Clinical & Interpretive

Clinical Information

Beta-galactosidase is a lysosomal enzyme responsible for catalyzing the breakdown of gangliosides. Isolated deficiency of this enzyme is expressed clinically as 2 different autosomal recessive diseases, GM1 gangliosidosis and Morquio syndrome B (mucopolysaccharidosis IVB [MPS IVB] or Morquio B). Galactosialidosis (GS) is associated with a combined deficiency of beta-galactosidase and neuraminidase secondary to a defect in protective protein cathepsin A. Enzymatic testing is not reliable for carrier detection of these conditions.

In GM1 gangliosidosis, reduced or absent beta-galactosidase activity leads to the accumulation of GM1 gangliosides, oligosaccharides, and keratan sulfate. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation. Type 1, or infantile onset, typically presents between birth and 6 months of age with a very rapid progression of hypotonia, dysostosis multiplex, hepatosplenomegaly, central nervous system degeneration, and death usually by 1 to 2 years of age..Type 2 is generally classified as late infantile or juvenile with onset between 7 months and 3 years of age presenting with developmental delays and a slower progression. Type 3 is an adult or chronic variant with onset between 3 and 30 years of age and is typically characterized by slowly progressive dementia with parkinsonian features and dystonia. The incidence has been estimated to be 1 in 100,000 to 200,000 live births.

In Morquio B, reduced or absent beta-galactosidase activity leads to the accumulation of glycosaminoglycans, particularly keratan sulfate, in lysosomes and interferes with normal functioning of cells, tissues, and organs. Morquio B typically manifests as a systemic skeletal disorder with variable severity ranging from early severe disease to a later

onset attenuated form. Virtually all patients have dysostosis multiplex and short stature along with other symptoms that may include coarse facies, hepatosplenomegaly, hoarse voice, stiff joints, cardiac disease, but no neurological involvement.

Galactosialidosis is an autosomal recessive lysosomal storage disease caused by variants in the cathepsin A gene, *CTSA*, resulting in a combined deficiency of the enzymes beta-galactosidase and neuraminidase. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation. Typical clinical presentation includes coarse facial features, cherry-red spots, and skeletal dysplasia. The early infantile form is associated with fetal hydrops, visceromegaly, skeletal dysplasia, and early death, while the late infantile form is characterized by short stature, dysostosis multiplex, coarse facial features, corneal clouding, hepatosplenomegaly, and/or heart valve problems. Individuals of Japanese ancestry make up the majority of patients with the juvenile/adult form of GS and typically develop symptoms after 4 years of age. These include neurologic degeneration, ataxia, and angiokeratomas.

A diagnostic workup in an individual with GM1 gangliosidosis, Morquio B, or GS typically demonstrates decreased beta-galactosidase enzyme activity in leukocytes or fibroblasts; however, additional testing and consideration of the patient's clinical findings are necessary to differentiate between these conditions. Follow-up testing may include LSDS / Lysosomal Storage Disorders Screen, Random, Urine, which analyzes urine mucopolysaccharides, oligosaccharides, ceramide trihexosides, and sulfatides. The LSDS test can help differentiate between the 3 conditions to guide physicians in choosing the best confirmatory molecular testing option. See Lysosomal Storage Disorders Diagnostic Algorithm, Part 1 .

Reference Values

> or =5.0 nmol/hour/mL
An interpretive report will be provided.

Interpretation

Results below 5.0 nmol/hour/mL in properly submitted specimens are consistent with beta-galactosidase deficiency (GM1 gangliosidosis, Morquio syndrome B, or galactosialidosis). Further differentiation between GM1, Morquio syndrome B, and galactosialidosis is dependent on the patient's clinical findings and results of additional biochemical testing.

Normal results (> or =5.0 nmol/h/mL) are not consistent with beta-galactosidase deficiency.

Cautions

This test cannot reliably determine carrier status.

This test does not differentiate between GM1 gangliosidosis, Morquio syndrome B, and galactosialidosis.

Clinical Reference

1. Suzuki Y, Nanba E, Matsuda J, et al: Beta-galactosidase deficiency (beta-galactosidosis): GM1 gangliosidosis and Morquio B disease. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 5, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547263
2. Regier DS, Tifft CJ: GLB1-related disorders. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2013. Updated August 29, 2019. Accessed January 5, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK164500

3. d'Azzo A, Andria G, Bonten E, Annunziata I: Galactosialidosis. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 5, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225547663
4. Arash-Kaps L, Komlosi K, Seegraber M, et.at: The clinical and molecular spectrum of GM1 gangliosidosis. Pediatr. 2019 Dec;215:152-157.e3. doi: 10.1016/j.jpeds.2019.08.016

Performance

Method Description

Whole blood collected in ACD or EDTA anticoagulant tubes is spotted onto filter paper and dried overnight. A one-eighth inch (3-mm) disk is punched out of the dried blood spot into a 96-well, round-bottom plate with citrate-phosphate buffer as elution liquid and 4-methylumbelliferyl-beta-D-galactopyranoside in water as the substrate. A blank is prepared using only elution liquid, substrate, and filter paper punches containing no blood. All patients, controls, and blank are set up in duplicate. After the incubation period, the liquid from the plate is transferred to a 96-well, flat-bottom black plate. A calibration curve is prepared and analyzed on every plate to calculate enzyme activity results, based on fluorescence units in patient wells vs calibrators. The calibration is derived from 4-methylumbelliferone (4-MU) that is serially diluted manually in the plate with the highest calibrator being equivalent to an enzyme activity of 10.4 nmol/hour/mL. Stop buffer is added to all wells (patients, quality controls, blanks, calibrators). The plate is then read on the spectrofluorometer. Fluorescence readings for duplicate wells are averaged, and the average fluorescence is used to calculate the enzyme activity result.(Civallero G, Michelin K, de Mari J, et al: Twelve different enzyme assays on dried-blood filter paper samples for detection of patients with selected inherited lysosomal storage diseases. Clin Chim Acta. 2006 Oct;372(1-2):98-102; Cowan T, Pasquali M: Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KD, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

PDF Report

No

Day(s) Performed

Wednesday

Report Available

8 to 15 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BGAW	Beta-Galactosidase, B	16454-1

Result ID	Test Result Name	Result LOINC® Value
60987	Beta-Galactosidase, B	16454-1
34427	Reason for Referral	42349-1
34432	Reviewed By	18771-6
34428	Interpretation	69047-9